United States Department of Agriculture
Agricultural Marketing Service
STOP 0268 – Room 4008-S
1400 Independence Avenue, SW.
Washington, D.C. 20250-0200

MEMORANDUM

DATE: March 9, 2006

TO: National Organic Standards Board

FROM: Valerie Frances
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National Organic Standards Board
National Organic Program

SUBJECT: Evaluation of the NOSB Recommendation on the Definition of Synthetic

This evaluation includes a number of technical, organizational, and editorial suggestions to improve clarity and utility of the recommendations. We also comment on the overarching approach proposed by NOSB to elaborate on the relationship between "synthetic" and the processes of "extraction" and "formulation." Our comments discuss difficulties that may arise through practical application of the NOSB's approach, and we provide suggestions intended to avoid these potential difficulties. In a separate document, we provide an alternative approach for determining whether or not a substance is synthetic or non-synthetic. This alternative approach is based on the NOSB recommendation and is consistent with the comments provided below.

General Comments

- The introduction does not make it clear why the additional guidance is needed to supplement the OFPA definition of "synthetic." The introduction section should be expanded to more fully explain the purpose of the recommendation and its context.

- The organization of the recommendation could be improved. For example, some sections of the recommendation simultaneously define key terms and advance interpretations of policy. To the extent possible, the guidance should be organized into a simple logical sequence. For example, the introduction should lay out the contents of the recommendation, and new definitions should be presented separately from the discussion of their rationale and how they affect the meaning of "synthetic."

- As described below, the recommendation, as written, may be difficult to apply in some situations due to the ambiguity of some text and the very specific technical nature of some terms and phrases. Since uncertainties may arise in future applications of the recommendation, the recommendation should

include a clear explanation of the intent underlying each definition and policy position. Such explanations may be helpful for interpreting and applying the recommendation if unforeseen issues arise.

Specific Comments on each of the Numbered Items in the NOSB Recommendation

1. Comments on "Extraction"

- It is unclear why the footnoted definition from 1995 is provided or why the 1995 definition is deficient.

- Consider a separate definition of "natural source" so that the phrase "naturally occurring plants, animals, or mineral sources," which is a phrase from the OFPA definition of "synthetic," does not have to be repeated twice in the definition of "extraction."

- Although microbiological sources (e.g., of streptomycin and tetracycline) are not included among the natural sources specified in the definition of "extraction," they are included in footnote 1 of the NOSB recommendation. It appears that microbiological sources are not included in the NOSB recommendation to be consistent with the OFPA definition of "synthetic." However, a discussion of the new definition should explain the rationale for this exclusion. If the meaning of "natural source" needs further refinement, it should addressed separately (i.e., not within the context of "extraction").

- Fungal sources are not included among the natural sources listed in the OFPA definition of synthetic, the NOSB definition of "extraction," or footnote 1. Arguably, fungi could be grouped with "microbiological sources." The NOSB recommendations should include separate and specific clarification or whether or not fungal material is a natural source.

- As written, the definition of "extraction" conveys three separate ideas relevant to the overall purpose of the NOSB recommendation. In addition to defining "natural source" and the process of "extraction," it explains the conditions under which an extracted substance can and would be considered nonsynthetic. If possible, this part of the recommendation should be broken down further so that each paragraph defines no more than one relevant term or concept. For example, the definition of "extraction" could be reduced to "the removal of a substance from a natural source by any chemical (e.g., solvent extraction, chemical precipitation) or physical (e.g., mechanical pressure, centrifugation, heating) manner and with any substance."

- The parenthetical "i.e." after "physical process" should be "e.g."

- The term "insignificant levels" of substances used in the extraction process is vague and should be defined more specifically. Due to the variety of

circumstances in which this definition would be applied, it may need to be a qualitative description of the NOSB's intent rather than a specific, quantitative analytical level.

2. Comments on "Formulation or Manufacturing"

- This section of the recommendation appears intended to accomplish the following:

  – Distinguish "formulation" as a process separate from "extraction" and "processing;"

  – Provide a definition for "formulation;" and

  – Explain the relationship between "formulation" and "synthetic."

  To clarify and emphasize each of these three closely-related but distinct topics, they should be separated and addressed in sequence.

- Although the OFPA definition of "synthetic" refers to "formulation or manufacturing," the precision of the terminology would be sharpened by defining one specific term ("formulation") rather than "formulation or manufacturing." "Manufacturing" could be described as a synonym in the same way that the OFPA describes "natural" as a synonym of "nonsynthtetic."

- The current text does not directly define "formulation." Based on the text in the NOSB recommendation, the following definition seems appropriate: "Formulation" is defined as the manufacture of an agricultural or handling input that is derived from a substance extracted from a natural source or produced by a naturally occurring biological process. Formulation is distinct from the processes of "extraction" and "processing," which are defined separately.

- This part of the NOSB recommendation clarifies the distinction between "formulation" and "processing." To avoid potential confusion, therefore, the definition of "formulation" should not use the word "processing" in its general meaning.

- The first sentence in this section of the NOSB recommendation refers to chemical changes that may happen when extracted chemicals are "processed, formulated, or manufactured." To enhance the distinction between these terms, the significance of chemical changes during "processing" should be discussed separately from chemical changes during "formulation."

- The recommendation says that a formulated product would be synthetic if any "chemical reaction" occurred during formulation. Use of the specific term

"chemical reaction" may be problematic in practice, particularly for substances that are not a single chemical species or that consist of large complex organic molecules (e.g., plant extracts, humic acids). This subject is discussed further in Section 4 of this memorandum.

3. Comments on the Definition of "Processing"

This section of the NOSB recommendation restates the existing definition of "processing" from the OFPA and the NOP rule. The purpose of including this definition, as stated in the "formulation and manufacturing" section of the NOSB recommendation, is to clarify the distinction between "processing" and "formulation." Because this definition is not a new concept advanced by this NOSB recommendation, it should be cited in the context of the relevant discussion rather than placing it as a stand-alone item. To emphasize that it is not a refinement or new definition, the existing definition should be quoted, cited, and perhaps indented or italicized.

4. The Definition of "Chemical Reaction"

The NOSB recommendation would consider any substance to be synthetic if it undergoes any chemical reaction during extraction or formulation. "Chemical reaction" is defined as "when one or more atoms are removed or added to a molecule." Examples of types of reactions identified in the NOSB recommendations include:

(1) Addition or combination reactions;
(2) Decomposition reactions; and
(3) Displacement reactions; and
(4) Protein configuration changes.

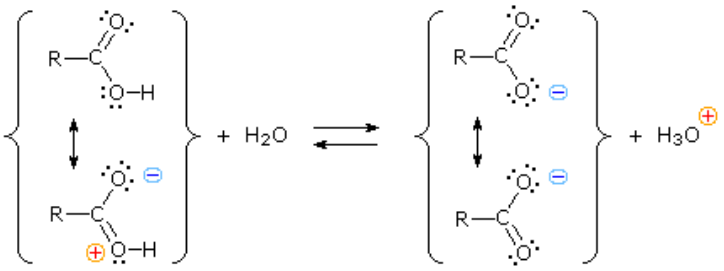
Although this definition is technically accurate, its use as a test to define whether a naturally occurring chemical is rendered synthetic is likely to be problematic in some cases, due largely to the specificity of this language. This approach may be more suitable for small, chemically stable and uniform substances (e.g., most minerals and simple inorganic compounds). Difficulties are likely to arise, however, when the approach is applied to more complex substances. Some potential complications are listed here:

- **Complex and non-specific substances.** Many substances that might be extracted from biological sources, such as proteins, lipids, or polysaccharides, are large organic molecules composed of a basic structural arrangement of primarily carbon atoms to which multiple functional groups are attached. Large organic chemicals often cannot be described by exact atomic composition or molecular weight. For example, the functional groups can vary without changing identity of the whole molecule. In addition, natural polymers, which are long chains of repeating molecular subunits that are not necessarily identical, can vary in chain length, as well as the number, position, and makeup of functional groups. For these large biomolecules, it may not be possible to determine whether "one or more atoms are removed or added"

because they are very complex and are not compositionally identical. (Note, however, that such substances *can* be assigned a separate CAS number; e.g., carrageenan gum, 9000-07-1; *Ascophyllum Nodosum* extract, 84775-78-0).

- **"Micro-scale" vs. "macro-scale" stability.** The approach taken in the recommendation seems to envision molecules as more static than they really are. Except for the most stable chemicals, molecules are constantly reacting (e.g., in a dynamic equilibrium). This is true even for substances that are considered to be quite stable on a "macro-scale." The molecules in a substance are continually in motion, colliding and reacting with other molecules. This behavior is most readily apparent in substances that exist as a gas or in solution (or as a pure liquid), but it occurs in solids as well (generally to a lesser degree). The range and rate of potential reactions depends on the chemicals present, temperature, pressure, and other factors. This dynamic nature is particularly true of large, complex organic molecules (e.g., gellan gum, humic acids, carrageenan gum) that may have numerous, potentially reactive functional groups. Therefore, the approach taken should recognize that chemicals may simultaneously exist in more than one related form in the natural source. Chemical reactions may occur, detected or not, during extraction or formulation that probably would not conflict with the intent underlying NOSB recommendation.

  For example, natural organic acids include those that contain one or more carboxylic acid functional group(s). In an aqueous solution, as shown below,[1] a resonance form of the carboxyl group can result in the loss of the hydrogen bonded to the carboxylate oxygen and the formation of an ionized form of the acid.



  The extent to which the forward reaction in this equilibrium occurs depends on the acidity of the solution and other factors. Although this reaction may not change nature of the substance (and may not occur very much under certain conditions), it will occur to some extent for all carboxylic acids and could be interpreted as "the removal of an atom [i.e., a hydrogen atom] from a molecule."

[1] Source of illustration: http://www.cem.msu.edu/~reusch/VirtualText/crbacid1.htm

- **Uniformity of a substance.** The "chemical reaction" test may have to be applied to mixtures comprised of various chemical substances (e.g., fish oil, botanical extracts). Because the composition of these mixtures may vary among different samples, and because the individual constituents may be complex biomolecules, it may be difficult to determine whether extraction or formulation has resulted in a "chemical reaction." Subtle chemical reactions (e.g., removal of an acetate group from an acetate ester) would be particularly difficult to identify. As mentioned in the previous bullet, such reactions will occur "naturally" to some extent even when they are not thermodynamically favored (e.g., for the ester example, without the addition of a basic reagent that might lead to significant deesterification). In a complex organic substance that occurs as a mixture, changes on the molecular level may occur even when they are not apparent.

- **Detection of a "new" molecule.** Because the product of a "chemical reaction" may be a form of a new chemical or a form of the starting chemical that occurs in mixture with the starting chemical in its natural source, it may be difficult to determine whether a "chemical reaction" has occurred merely by analyzing the substance.

- **Natural stability.** Some nonsynthetic substances may decay spontaneously (e.g., from exposure to light) over time. Similarly, some substances may decay or react not because of an intentional formulation process, but only because they have been removed from the chemical or physical environment of their natural source (e.g., on contact with air or moisture or due to changes in temperature). If a reaction involved in such a case is not a "naturally occurring biological process" (i.e., one that occurs *in vivo*), then the products presumably would be synthetic because a chemical reaction (decomposition) has occurred. It is unclear whether the NOSB approach intends for these types of reactions to always render synthetic products. Additional refinement of the recommendation may be needed to address these types of reactions. Related to this issue, it may be difficult, in some cases, to distinguish spontaneous decay or chemical reactions from chemical reactions caused by extraction or formulation methods (see the example presented in the previous bullet regarding uniformity of a substance).

- **Isomerization.** The NOSB does not include isomerization (including conformational isomerism) among the types of chemical reactions that would render a chemical synthetic. Isomerization occurs when a chemical compound undergoes a structural rearrangement without any change in its net atomic composition. Presumably, isomerization was not mentioned because it does not involve the net addition or removal of atoms. However, isomers can have different properties. The recommendation should specifically discuss when an isomer of a nonsynthetic substance would or would not be considered synthetic.

One option to address these limitations would be to refine the definition of "chemical reaction" to permit certain types or ranges of reactions that would not go against the underlying objective of the NOSB recommendation. This option would be challenging to develop (due partly to the wide range of reactions that would need to be considered) and may result in technically complicated and difficult-to-use criteria. A second option would be to replace the mechanistic approach with an empirical approach. For example, the relationship between "extraction" and "synthetic" could be defined in terms of changes in the substance's technical or functional properties. For example, it may be reasonable to allow chemical reactions during extraction or processing that: (1) result from a "naturally occurring biological process" or (2) do not result in the chemical becoming a different "substance" as currently defined by the NOSB recommendation. These criteria are examples; further criteria could be developed to ensure that the underlying intentions of the NOSB recommendation are achieved.

NOSB's underlying intention of the recommendation apparently is to ***prevent*** any of the following from occurring:

- The transformation, during extraction or formulation, of a nonsynthetic substance into a different "substance;"

- The alteration of a nonsynthetic substance such that it retains its identity but assumes a chemical form that does not occur in nature;

- The alteration of a nonsynthetic substance such that it retains its identity but does not retain important functional properties (e.g., nutritional value, flavor, efficacy for an intended use);

- The contamination of a nonsynthetic substance during extraction by a "significant level" of a synthetic substance that is not on the National List. "Significant level" in this context could be defined as an amount capable of producing a functional or technical effect.

- The commingling of a nonsynthetic substance during formulation with a synthetic substance that is not on the National List.

A direct statement of the objectives and intentions of the recommendation would be helpful to resolve any unforeseen uncertainties that may arise in their application to specific substances.

5. "Substance"

"Substance" is not defined by the OFPA or the NOP rule. The definition of a substance as a compound or element that has a distinct identity (e.g., separate Chemical Abstract Society (CAS) number, Codex International Numbering System (INS) number, or FDA or other agency standard of identity) is scientifically sound. This definition

would allow for minor variations in the atomic composition or molecular weight of complex biomolecules.

In the second sentence of this section, the phrase “nonorganic substance” is used, presumably to indicate the use of a synthetic substance. This should be clarified to avoid confusion with the term “nonorganic” used in chemistry to refer to chemicals that are inorganic (i.e., generally, compounds that do not consist of carbon atoms, such as most minerals).

In addition to defining “substance,” this part of the NOSB recommendation clarifies that any synthetic substance for use in crop and livestock production and any nonorganic substance for use in processing must be separately listed in the National List for use in organic production or handling. This concept should be presented separately from the definition of “substance.”

6. “Substance Created by Naturally-occurring Biological Processes”

This portion of the NOSB recommendation is scientifically sound and consistent with the OFPA and the NOP rule. The definition of a “naturally occurring biological process” should be separated from the policy stating that substance created by naturally occurring biological processes are not considered synthetic.

7. “Nonsynthetic (natural)”

The definition of nonsynthetic in the NOSB recommendation is the same definition provided by the OFPA and the NOP rule.